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Review Article

REACTIVE OXYGEN SPECIES: A BOON OR BANE TO HUMAN HEALTH

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ABSTRACT
In recent times free radicals have remarkable significance in the field of medicine and molecular biology. Free radicals can be either harmful or helpful to the body. Where there is an imbalance between formation and removal of free radicals then a condition called as oxidative stress is developed in body. To counteract these free radicals body has protective antioxidant mechanisms which have abilities to inhibit the production of ROS by direct scavenging, decrease the amount of oxidants in and around our cells, prevent ROS from reaching their biological targets, limit the propagation of oxidants such as the one that occurs during lipid peroxidation, and prevent oxidative stress thereby preventing the aging phenomenon.
Keywords: Reactive oxygen species, free radicals, oxidative stress, antioxidants

INTRODUCTION

Oxygen is essential for life but its high concentration can be toxic, since the molecular oxygen can be reduced to ROS by definite metabolic pathways[1]. Reactive oxygen species (ROS) have a crucial role in human physiological and pathophysiological processes[2]. Reactive oxygen species are related with free radicals in biological systems, even non-radical compounds such as singlet oxygen and hydrogen peroxide. Generally they are highly reactive, unstable and animated molecules[3]. ROS are generated as by-products of cellular metabolism, primarily in the mitochondria[4] and include free radicals such as superoxide anion (O_2–•), perhydroxylradical (HO_2•), hydroxylradical (•OH), nitricoxide (NO) and other species such as hydrogenperoxide (H_2O_2), singlet oxygen ($^1O_2$), hypochlorous acid (HOCl), and peroxynitrite ($ONOO^-$)[5]. In normal cell function ROS is generated constitutively by non-phagocytic cells and inresponse to injury, trauma or infection by phagocytic cells[6,7]. A common functionalattribute of the two sources of ROS is that moderate amounts are largely associated withsignaling activity while increasing amounts is important in cellular defense and or repair[8]. Moderate amounts of ROS are generated through electron transport, vascular smoothmuscle cell (VSMC) and endothelial cell (EC) activities[9]. Other cellular sources of ROS that may be limited by the changes in cellular metabolic activity include lipoxygenases, cyclooxygenase, cytochrome P450 enzyme activities and lipid peroxidation[10]. To prevent the damage from ROS, cells possess several antioxidant enzymes such as superoxide dismutases, Mn SOD and Cu/Zn SOD, which are located in the mitochondria and the cytosol respectively, where they convert superoxide into hydrogen peroxide[11]. The decomposition of hydrogen peroxide to water and oxygen is further catalyzed by catalase. Another antioxidant defense mechanism includes non enzymatic antioxidants such as glutathione (GSH), which functions in the cellular thiol/disulfide system[12,13]. According to the clinical studies, reactive oxygen species may cause many degenerative diseases, such as atherosclerosis, cancers, vasospass, stroke, trauma, asthma, heart attack, hyperoxia, arthritis, age pigments, cataract genesis, retinal damage, dermatitis, liver injury, hepatitis, and periodontis[14,15]. This review briefly enumerates the role of free radicals and reactive oxygen species in health and disease.

Oxidative stress

Oxidative stress corresponds to an imbalance between the rate of oxidant production and that of their degradation[16]; when this occurs, oxidation of important macromolecules including proteins, lipids, carbohydrates, and DNA ensues[17]. According to Sies (1985)[18] "oxidative stress" is defined as "a disturbance in the pro oxidant–antioxidant balance in favor of the former". Therefore an updated definition of oxidative stress could be "severe disturbance in the pro oxidants–antioxidants balance in favor of the former, thus leading to a potential damage to the cells and organs"[19]. Essentially, "oxidative stress" occurs when the formation of bioactive oxidation products greatly overwhelms the capacity of endogenous cellular antioxidant defense system. The resulting damage to cells and organs may activate and/or accelerate disease processes[20].

Antioxidants

Living tissues have a control mechanism to keep ROS in balance. When ROS are generated *in vivo*, many antioxidants come into play. Their relative importance depends upon which ROS are generated, how and where they are generated, and which target of damage is considered[21]. Our body defends itself from these phenomena via endogenous antioxidants[21-23]. However, when endogenous antioxidants become insufficientor imbalanced in defense against oxidants, exogenous antioxidants may help restore the balance. Antioxidants inhibit the production of ROS by direct scavenging, decrease the amount of oxidants in and around our cells, prevent ROS from reaching their biological targets, limit the propagation of oxidants such as the one that occurs during lipid peroxidation, and prevent oxidative stress thereby preventing the aging phenomenon[24].

ROS in health and disease

At low, regulated levels, ROS are involved in many vital physiological processes. They have a role in various signaling

cascades, such as response to growth factor stimulation and control of inflammatory responses[25]. They participate in the regulation of many cellular processes, including differentiation, proliferation, growth, apoptosis, cytoskeletal regulation, migration and contraction[26]. It has been observed that whenever either the level of the cellular antioxidant systems goes down or when the ROS reach abnormally high levels, oxidative damage to the cells occurs, finally leading to several pathological conditions[27]. About 100 disorders, like rheumatoid arthritis, hemorrhagic shock, cardiovascular diseases, cystic fibrosis, metabolic disorders, neurodegenerative disease, gastrointestinal ulcerogenesis and AIDS, have been reported as the ROS mediated disorders[27-32]. Some specific examples of the ROS mediated diseases are Alzheimer's disease[33], Parkinson's disease[30,34]. Oxidative modification of low-density lipoprotein in atherosclerosis[35], cancer[36,37], Down's syndrome[38] and ischemic reperfusion injury in different tissues including heart, brain, kidney, liver, and gastrointestinal tract[39]. Among these, role of ROS in atherosclerosis[40] and ischemic injury in heart [41] and brain[42] have been studied extensively[28]. The major role played by ROS in stress induced gastric ulcer and inflammatory bowel diseases has been recently established[43,29,44,45]. The involvement of ROS in aging has been documented as well[46-48].

Diabetes mellitus (DM)

Diabetes mellitus (DM) is a syndrome characterized by abnormal insulin secretion, derangement in carbohydrate and lipid metabolism and is diagnosed by the presence of hyperglycemia. Diabetes is a major worldwide health problem predisposing to markedly increased cardiovascular mortality and serious morbidity and mortality related to development of nephropathy, neuropathy and retinopathy[49]. The prevalence of type 2 DM among adults varies from less than 5 % to over 40 % depending on the population in question[49]. Due to increasing obesity, sedentariness and dietary habits in both Western and developing countries, the prevalence of type 2 DM is growing at an exponential rate[50]. Increased oxidative stress as measured by indices of lipid peroxidation and protein oxidation has been shown to be increased in both insulin dependent diabetes (IDDM), and non-insulin dependent (NIDDM)[51-62], even in patients without complications. Increased oxidized low density lipoprotein (LDL) or susceptibility to oxidation has also been shown in diabetes[53,55-57,59,60].

Skinaging

Skin, like all other organs, undergoes changes due to aging. Skin aging appears to be the result of two types of aging, "intrinsic" and "extrinsic". "Intrinsic" structural changes occur as a consequence of physiological aging and are genetically determined. However, it is very difficult, if not impossible to separate "intrinsic" aging from a variety of other factors clearly contributing to aging, such as smoking, sun exposure, alcohol consumption, dietary habits, and other environmental and lifestyle factors[61,62]. The underlying mechanism of both processes is increased oxidative stress, which is probably the single most harmful contributor to skin aging, leading to loss of cells and the extracellular matrix as the most prominent features of chronologically aged skin[63]. The clinical manifestations of intrinsic aging are fine wrinkles, thin and transparent skin and loss of underlying fat leading to hollowed cheeks and eyesockets, dry anditchy skin, inability to perspire sufficiently, hair graying, hair loss or hirsutism, and thinning of nail plates[64].

Eye diseases

Oxidative stress has been associated in the pathogenesis of several eye conditions such as corneal disease, cataract, macular degeneration, diabetic retinopathy and retinitis pigmentosa[65-70].

Cataract

ROS and oxidative stress are involved in many ocular diseases including cataract[70]. Production of ROS and reduction of endogenous antioxidants both contribute to cataract formation[68]. According to Berthoud and Beyer (2009)[71], oxidative stressinduced damage to lens gap junctions and consequent altered intercellular communication may contribute to cataract formation. Lipid peroxidation has been proposed as a causative factor of cataract[65]. Sawada *et al*.[72] found a significant increase in superoxide dismutase activity and protein level in nuclear cataracts, suggesting the involvement of oxidative stress. However, with ageing, accumulation of oxidized lens components and decreased efficiency of repair mechanisms can contribute to the development of cataract[71].

Macular degeneration (AMD)

Age related macular degeneration is a leading cause of blindness in the developed countries[73]. The retina is particularly susceptible to oxidative stress because of its high oxygen consumption, its high proportion of polyunsaturated fatty acids and its exposure to visible light[74]. Several risk factors for AMD such as genetics, age, exposure to sunlight and smoking have been reported[73]. The macular pigment formed by two dihydroxyl carotenoids, lutein and zeaxanthin is a natural barrier protecting the macula against oxidative stress[75]. However, retinal factors such as intense oxygen metabolism, exposure to ultraviolet radiation, high concentration of polyunsaturated fatty acids and presence of photosensitizers may increase the production of ROS[75].

Atherosclerosis

Atherosclerosis is a chronic inflammatory process affecting large and mediumsized arteries throughout the cardiovascular system[76]. The early stages of atherosclerosis are similar to the reaction noted in asthma. It consists of infiltration of the affected site by T-lymphocytes and monocytes, which then transforms into macrophages, followed by proliferation of fibrous tissue[77]. Eventually in its natural progression, calcification of the atheromatous plaque occurs. These plaques may partially or totally block the blood's flow in arteries which results in heart attack or stroke. According to the theory of oxidative stress, atherosclerosis is the result of the oxidative modification of low density lipoproteins (LDL) in the arterial wall by reactive oxygen species[78]. These processes are triggered by risk factors, including the expression of adhesion molecules, proliferation and migration of smooth muscle cells, apoptosis of endothelial cells, oxidationof lipids, activation of metalloproteinase and alteration of vasomotor activity[77].

CONCLUSION

In general ROS enables normal physiological cellular functions to be sustained and provides defense against invading organisms. When ROS is in excess shown as oxidative stress, it plays a destructive role leading to cellular

damage. However, various genetic or environmental conditions sometimes lead to an imbalance between the production and the decomposition of these reactive intermediates that lead to deleterious consequences. Conversely, an adequate level of certain ROS can have a physiological role, as for instance the catalysis of many biochemical reactions or the defense against invading pathogens.

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